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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/666,722	09/18/2003	Lee Martin Greenberger	AM101032	9014

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EXAMINER	
BETTON, TIMOTHY E	
ART UNIT	**PAPER NUMBER**
1614	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	04/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/666,722	GREENBERGER ET AL.	
	Examiner	Art Unit	
	Timothy E. Betton	1614	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 December 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-81* is/are pending in the application.

4a) Of the above claim(s) *16-18,20,29-38,40-48,50, and 60-72* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-15,19,21-28,39,49,51-59 and 73-81* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *5 sheets*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Applicant's election with traverse in the reply filed on 20 December 2006 is acknowledged.

The requirement is still deemed proper and is therefore made FINAL.

Status of the Claims

Claims 1-15, 19, 21-28, 39,49, 51-59 and 73-81 are pending for prosecution on the merits.

Claim Rejection- 35 USC §, 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims1-15, 19, 21-28, 39,49, 51-59 and 73-81 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for certain synthetic analogues of the tripeptide hemiasterlin, does not reasonably provide enablement for the Formula II hemiasterlin derivative the applicant has elected disclosed within instant claim 73 for the same therapeutic use. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

The factors to be considered in determining whether a disclosure meets the enablement requirement of 35 U.S.C. 112, first paragraph, have been described in In re

Wands, 8 USPQ2d 1400 (Fed. Cir. 1988). Among these factors are: (1) the nature of the invention; (2) the state of the prior art; (3) the relative skill of those in the art; (4) the predictability or unpredictability of the art; (5) the breadth of the claims; (6) the amount of direction or guidance presented; (7) the presence or absence of working examples; and (8) the quantity of experimentation necessary. When the above factors are weighed, it is the Examiner's position that one skilled in the art could not practice the invention without undue experimentation.

(1) The nature of the invention:

The instant invention is directed toward a method of treating, inhibiting the growth of, or eradicating a tumor in a mammal. It involves the use of chemotherapeutics, which make the nature of the invention necessitate adequate and proper enablement as required.

(2) The state of the prior art

The prior art does not teach the specific hemiasterlin moiety in claimed invention elected by applicants. Scope of enablement is often difficult to ascertain and/or produce due to a lack of teaching in the pertinent prior art.

(3) The relative skill of those in the art

The relative skill of those in the art of neuropharmaceuticals is very high.

(4) The predictability or unpredictability of the art

The unpredictability of the pharmaceutical art is very high due to the multiplicity of susceptibilities, properties and characteristics of any one hemiasterlin derivative. Applicants' elected hemiasterlin derivative is the instant example. Hemiasterlin derivatives are designed to decrease multiple drug resistance experienced by the initial

administration of antimicrotubule inhibitors. Unpredictability is high due to reasons disclosed above and also in association with specific stages or cellular phases of cancer growth, that quickly develop resistive characteristics.

Additionally, challenges to treatment are due to limited quantities of hemiasterlins at times, which are not enabling in scope with the claimed invention. Synthetic methods for producing said hemiasterlin must be conducted in such a way to ensure claimed therapeutic and preventative properties. (Loganzo et al, HTI-286, a Synthetic Analogue of the Tripeptide Hemiasterlin, Is a Potent Antimicrotubule Agent that Circumvents P-Glycoprotein-mediated Resistance *in Vitro* and *in Vivo*, (2003) Cancer Research 63, 1838-1845, printed pages 1-17, especially page 3).

(6) The amount of direction or guidance presented

The amount of direction or guidance needed is not sufficient in order to determine scope of enablement for a said drug agent being indicated for treating and/or inhibiting cancerous tumors.

(7) The presence or absence of working examples

The presence of working examples is absent. There is nothing in the instant specification that discloses a practicing method of treating the growth of cancerous tumors in a mammal with inherent or acquired resistance.

(8) The quantity of experimentation necessary

The quantity of experimentation needed to be performed by one skilled in the art is yet another factor involved in determining whether "undue experimentation" is required to make and use the instant invention. "'The test is not merely quantitative, since a

considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.'" In re Wands, 858 F.2d 737, 8 USPQ2d 1404 (citing In re Angstadt, 537 F.2d 489, 502-04, 190 USPQ 214,218 (CCPA 1976)). For these reasons, one of ordinary skill in the art would be burdened with undue experimentation to determine if the elected hemiasterlin (Formula I) is allegedly effective to treat any and all cancer-type disease states that would be enabled in this specification.

Claim Rejection- 35 USC §, 112, 1st Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 1 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

con, AA 4-2-07

The terms "inhibiting" and "eradicating" in claim 1 are relative terms, which render the claim not enabled. The terms "inhibiting" and "eradicating" are not defined by the claim in any requisite degree. Furthermore, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention.

The subject matter of the instant invention is directed toward treating cancer with claimed inventive central issue of inhibiting and/or eradication of a cancerous tumor. One of ordinary skill in the art instantly recognizes that due to the multiplicity of susceptibilities, properties, resistance factors, etc. of any and all cancerous disease states/conditions, the terms "inhibiting" and "eradication" have no factual basis either disclosed in the specification or instant claims. There is no definite degree described either in the instant claims or specification that suggests that invention is enabled for inhibiting and/or eradicating.

Response to Arguments

Applicants' remarks filed 20 December 2006 has been acknowledged. Applicants traverse several points following: 1. the lack of necessity of the restriction requirement by Examiner 2. the undue burden it would pose to applicant as opposed to Examiner to require restriction 3. Examiner's alleged failure to explain the reason it would be undue burden on Examiner. 4. Examiner's failure to clarify request of species.

Applicants' arguments are acknowledged, however are not found persuasive. Where there is a multiplicity of embodiments and/or species within the claims, restriction is proper. The necessity of a restriction requirement is determined by the Examiner. This multiplicity of embodiments thus poses an undue burden on the Examiner if all were to be searched and examined together. The burden upon the applicant is to adequately disclose what is the central issue of said claimed invention. The burden

upon the Examiner is to properly prosecute claims on the merits as have been adequately disclosed. Clarification of the election of species are disclosed as following:

1) The Examiner has requested election of a species for Group I. Applicants elect the species of Example 57:N,O,13,13-tetramethyl-L-tyrosyl-Nl-[(1 S,2E)-3-carboxy-l-isopropyl-2-butenyl]-N1,3-dimethyl-L-valinamide. Claims 1-15, 19, 21-28, 39, 49, 51-59 and 73-81 are believed to be readable on this species.

2) The Examiner has further required an election of a chemotherapy agent/antimicrotubule inhibitor or combination, which will be administered with the elected species. Applicants elect paclitaxel.

3) The Examiner also has required election of a tumor disease/condition. Applicants elect ovarian tumors.

4) The Examiner has required yet another election: Applicants are asked to elect one regimen species, i.e., treatment with the Formula II compound before, concurrently with, or after the chemotherapeutic agent. Applicants provisionally elect treatment with the Formula II compound after the chemotherapeutic agent.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Timothy E. Betton whose telephone number is (571) 272-9922. The examiner can normally be reached on Monday-Friday 8:30a - 5:00p.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin H. Marschel can be reached on (571) 272-0718. The fax phone

number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

TEB

4/2/07

ARDIN H. MARSCHEL
SUPERVISORY PATENT EXAMINER